Claims 61-70 have been added. Support for new Claims 61-70 can be found in the original claims. Hence, the amendments to Claims 1, 4-21 and 23-59, the cancellation of Claims 22 and 60, and the addition of Claims 61-70 do not constitute new matter, and thus entry is requested.

The Examiner is invited to contact the undersigned at his Washington telephone number on any questions which might arise.

Respectfully submitted,

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A P P E N D I X

Marked-Up Version of Changes

IN THE CLAIMS:

Claims 2-3, 22 and 60 are being cancelled.

The claims are amended as follows:

Claim 1. (Amended) [A] An isolated nucleotide [sequence] molecule coding for a protein present in invertebrate and/or vertebrate organisms, wherein said [nucleotide sequence coding for a] protein [comprising] has a positive function in [a regulatory pathway] the Wnt/Wg-pathway, and wherein said protein comprises a legless (lgs) gene product.

Claim 4. (Amended) The isolated nucleotide [sequence] molecule according to [claims 1-3] claim 1, wherein said [nucleotide sequence is coding for] lgs gene product is *Drosophila* Legless (Lgs) protein.

Claim 5. (Twice Amended) The isolated nucleotide [sequence] molecule according to claim 4, wherein said nucleotide [sequence] molecule comprises the nucleotide sequence [as] shown in Figure 2 (SEQ ID NO:1).

Claim 6. (Amended) The isolated nucleotide [sequence] molecule according to [claims 1-3] claim 1, wherein said [nucleotide sequence is coding for] lgs gene product is human Legless (hLgs) [proteins] protein.

Claim 7. (Twice Amended) The isolated nucleotide [sequence] molecule according to claim 6, wherein said nucleotide [sequence] molecule comprises the nucleotide sequence [as] shown in Figure 10A (SEQ ID NO:16).

Claim 8. (Twice Amended) [A] An isolated nucleotide [sequence] molecule [comprising] having at least 50% homology to

(a) the nucleotide sequences [sequence or stretches of the nucleotide sequence as] shown in [Figures] Figure 2 (SEQ ID NO:1) and Figure 10A (SEQ ID NO:16) or (b) complements or fragments thereof.

Claim 9. (Amended) The isolated nucleotide [sequence] molecule according to [any of claims 1 to 8] claim 8, wherein said fragments [of said sequence] are [used as] probes for use in hybridization assays.

Claim 10. (Amended) A vector comprising the [nucleic acid] nucleotide molecule according to [any of claims] claim 1 [to 8].

Claim 11. (Amended) The vector of claim 10, wherein said nucleotide molecule is operably linked to control sequences recognized by a host cell transformed with said vector.

Claim 12. (Amended) A host cell [containing] comprising the vector of [claims 10 and 11] claim 10, wherein said host cell is selected from the group consisting of mammalian, bacterial, yeast, plant and insect cells.

Claim 13. (Amended) [A] An isolated polypeptide encoded [derived from any of] by the nucleotide [sequences] molecule of [claims] claim 1 [to 8], derivatives, fragments and analogs thereof.

Claim 14. (Amended) The polypeptide of claim 13, wherein said polypeptide comprises [comprising the function of] Legless proteins.

Claim 15. (Amended) [A] An isolated polypeptide sharing one or more homologue amino acid domains with [the] a Legless protein and being a functional homologue of [legless] a Legless protein.

Claim 16. (Amended) The polypeptide according to claim 15, wherein said functional homologue is the hLgs/Bcl-9 protein or a

fragment thereof, and [comprising] has the function of a Legless protein in the Wnt-pathway.

Claim 17. (Amended) [Use of the polypeptide] A method for [according to any of claims 13-16 for the isolation of] isolating a Lgs-binding [proteins] protein comprising [by carrying out a co-immunoprecipitation assay] co-immunoprecipitating a Lgs-binding protein in a sample using the polypeptide of claim 13.

Claim 18. (Amended) A process for producing a polypeptide [according to claim 13 to 16] comprising culturing a [the] host cell [of claim 12] comprising the vector of claim 10, under conditions suitable for expression of said polypeptide and recovering said [protein] polypeptide or fragment thereof from the cell culture, wherein said host cell is selected from the group consisting of mammalian, bacterial, yeast, plant and insect cells.

Claim 19. (Amended) An antibody which specifically binds to the polypeptide [polypeptides] of [claims 13 to 16] claim 13, wherein said antibody is selected from the group consisting of polyclonal antibodies, monoclonal antibodies, humanized antibodies and single chain antibodies.

Claim 20. (Amended) A chimeric molecule comprising the polypeptide of [any of claims 13-16] claim 13 or a fragment thereof fused to a heterologous amino acid sequence.

Claim 21. (Amended) The chimeric molecule according to claim 20, wherein said heterologous amino acid sequence is selected from the group [comprising] consisting of an epitope tag sequence, a glutathione-S-transferase moiety, a thioredoxin moiety, and an antibody moiety.

Claim 23. (Amended) [A] An isolated peptide, comprising [a stretch of amino acids comprising] at least one sequence homology domain[,] which is common between [the] *Drosophila* Legless proteins and human Legless proteins.

Claim 24. (Amended) The peptide according to claim 23, wherein the [common domains from human Legless are derived from] human Legless proteins are hLgs-1 or hLgs/Bcl9.

Claim 25. (Amended) [Compound interfering] A compound which interferes with the binding of partner proteins to the [domains] at least one sequence homology domain according to claim 23 [claims 23-24 for inhibiting the interaction between partner proteins to these domains by exposing said domains to said compounds].

Claim 26. (Amended) The compound according to claim 25, wherein said partner proteins are selected from the group consisting of Dll1 and β-Catenin.

Claim 27. (Amended) The compound according to [claims 25 and 26] claim 26, wherein said [compounds are] compound is selected from [a] the group consisting of small peptides, synthetic polymers, and natural or synthetic chemical compounds.

Claim 28. (Amended) The compound according to [claims 25 and 26] claim 27, wherein said compound is a small peptide comprising the sequence homology domain 1 of figure 7B (SEQ ID NOs:2-3) or the sequence homology domain 2 of figure 7B (SEQ ID NOs:4-5).

Claim 29. (Amended) [Use of the compound according to claim 28 in a] A pharmaceutical composition for delivering said small peptide of claim 28 or [its relative nucleic acid sequence in an appropriate] a vector encoding the same, into a cancerous

cell comprising said small peptide or vector; and a pharmaceutically acceptable carrier.

Claim 30. (Amended) A synthetic molecule, wherein said molecule [simulating] simulates the function of Legless proteins in the Wnt pathway.

Claim 31. (Amended) An antagonist of the polypeptide of [claims 13-16] claim 13, wherein said antagonist is selected from the group [comprising] consisting of small bioorganic molecules, synthetic polymers, [or] and small polypeptides.

Claim 32. (Amended) An agonist of the polypeptide according to [claims 13-16] claim 13, wherein said agonist is selected from the group [comprising] consisting of small polypeptides, and small bioorganic molecules.

Claim 33. (Amended) A method of screening for agonists and/or antagonists of the polypeptide claimed in claim 13 [claims 13-16 for functional activity] comprising screening a chemical library for compounds which inhibit the interaction of Lgless proteins and a partner protein using a reagent that detects said interaction.

Claim 35. (Amended) An isolated antisense oligonucleotide [sequence derived from] which hybridizes to the nucleotide [sequences] molecule according to [claims] claim 1 [to 8].

Claim 36. (Amended) The antisense oligonucleotide [sequence] according to claim 35, wherein said oligonucleotide [sequence] hybridizes to RNA and/or genomic DNA encoding a vertebrate Lgs.

Claim 37. (Amended) The antisense oligonucleotide [sequence] according to [claims 35 and 36] claim 36, wherein said oligonucleotide [sequence] prevents translation of said RNA or transcription of said DNA.

Claim 38. (Amended) The antisense oligonucleotide [sequence] according to [claims 35 to 37] claim 35, wherein said oligonucleotide [sequence] comprises chemically modified nucleotides or nucleotide analogs.

Claim 39. (Amended) A method of treatment of [Use of the antisense oligonucleotides according to claims 35-38 in the therapy of] diseases caused by [an] over-activation of the Wg pathway comprising administering, to a subject in need of such treatment, a pharmaceutically effective amount of the antisense oligonucleotide of claim 35.

Claim 40. (Amended) [A] An isolated double-stranded RNA [sequence] molecule [derived from] corresponding to the nucleotide [sequences] molecule according to [claims] claim 1 [to 8], wherein said RNA molecule has [comprising] RNA interfering [activities] activity.

Claim 41. (Amended) The double-stranded RNA [sequence] molecule according to claim 40, wherein said double-stranded RNA [sequence] molecule is [able to] effective to induce degradation of lgs [single stranded] single-stranded RNA.

Claim 42. (Amended) A method [Use of the double-stranded RNA according to claims 40 and 41] for reducing lgs gene expression in an invertebrate or vertebrate organism or an invertebrate or vertebrate cell line comprising contacting said organism or cell line with an amount of said double stranded DNA molecule of claim 40 sufficient to reduce lgs gene expression therein.

Claim 43. (Amended) A pharmaceutical composition comprising an oligonucleotide derived from the nucleotide [sequence] molecule according to [any of claims] claim 1 [claims 1-8], and [further comprising an acceptable pharmaceutical] a

pharmaceutically acceptable carrier, wherein said oligonucleotide and said [pharmaceutical] carrier [being capable of passing] are passable through a cell membrane.

Claim 44. (Amended) A pharmaceutical composition [derived from] comprising the polypeptide of claim 16, and [further comprising an acceptable pharmaceutical] a pharmaceutically acceptable carrier, wherein said polypeptide [pharmaceutical composition being an oligonucleotide] and said [pharmaceutical] carrier are [capable of passing] passable through a cell membrane.

Claim 45. (Amended) The pharmaceutical composition according to [claims 43 and 44] claim 43, wherein said oligonucleotide [is capable of reducing] is effective to reduce [the] expression of a mammalian Lgs protein.

Claim 46. (Amended) The pharmaceutical composition according to [claims 43 to 45] claim 43, wherein said oligonucleotide is coupled to a moiety that inactivates mRNA.

Claim 47. (Amended) The pharmaceutical composition according to claim 46, wherein the moiety [inactivating] that inactivates mRNA is a ribozyme [(ribozyme is an enzyme)].

Claim 48. (Amended) The pharmaceutical composition according to [claims 43 to 47] claim 43, wherein the pharmaceutically acceptable carrier comprises a structure which binds [binding] to a receptor on a cell surface, wherein said structure [being] is taken up by the cell after binding to said receptor.

Claim 49. (Amended) The pharmaceutical composition according to [claims 43 to 46] claim 43, wherein said oligonucleotide is [the] a double stranded RNA molecule [of claims 37 and 38] derived from the nucleotide molecule according

to claim 1, wherein said RNA molecule possesses RNA interfering activity.

Claim 50. (Amended) The pharmaceutical composition according to claim 49, wherein the double stranded RNA molecule comprises 18 to 1000 nucleotides[, preferably 20 to 500 nucleotides, more preferably 20 to 50 nucleotides and most preferably 20 to 22 nucleotides].

Claim 51. (Amended) A [therapeutic] method for treatment of cell fate disorders comprising administering, to a subject in need of such treatment, a pharmaceutically effective amount of [the use of] a compound selected from the group consisting of Lgs proteins, homologues thereof, functional homologues, [nucleic acids] and nucleotide molecules encoding the same and/or fragments thereof [for the treatment of disorders of cell fate, comprising the administration of a therapeutic compound].

Claim 52. (Amended) The [therapeutic] method according to claim 51, wherein said [disorders of] cell fate disorders [being] are disorders in cell differentiation or proliferation.

Claim 53. (Amended) The [therapeutic] method according to claim 51, wherein said [comprising the administration of a therapeutic] compound is selected from the group consisting of invertebrate and vertebrate Lgs protein homologues or fragments thereof, antibodies, antibody fragments, Lgs antisense DNA, *lgs* antisense RNA, *lgs* double-stranded RNA, small peptides, and chemical or natural compounds [being capable of interfering] which interfere with Lgs function, synthesis and degradation.

Claim 54. (Amended) The [therapeutic] method according to claim 51 [claims 51-53], wherein the [therapeutic] compound is administered to treat a cancerous condition.

Claim 55. (Amended) The [therapeutic] method according to claim 51 [claims 51-53], wherein the [therapeutic] compound is administered to prevent progression from a pre-neoplastic or non-malignant condition to a neoplastic or malignant state.

Claim 56. (Amended) The [therapeutic] method according to claim 51 [claims 51-53], wherein the [therapeutic] compound is administered to treat a cancerous condition characterized by over-stimulation of the Wnt pathway.

Claim 57. (Amended) The [therapeutic] method according to claim 56, wherein the cancerous condition is selected from the group consisting of colon, breast, head and neck, brain, [tyroid] thyroid, medulloblastoma [or] and skin cancer.

Claim 58. (Amended) The [therapeutic] method according to claim 51 [claims 51-53], wherein the [therapeutic] compound is administered to treat a blood disease.

Claim 59. (Amended) The [therapeutic] method according to claim 51 [claims 51-53], wherein the [therapeutic] compound is administered to promote tissue regeneration and repair.

New Claims 61-70 are being added.